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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/795,933	03/08/2004	Jan Zavada	D-0021.2-2	2689

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/795,933	ZAVADA ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-35 and 39-55* is/are pending in the application.

4a) Of the above claim(s) *41-55* is/are withdrawn from consideration.

5)☒ Claim(s) *31-35 and 53-55* is/are allowed.

6)☒ Claim(s) *39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on September 13, 2006.

Currently, claims 31-35 and 39-55 are pending. Applicants have cancelled claims 1-30 and 36-38 and elected claims 31-35 and 53-55 on March 16, 2006.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Terminal Disclaimer

The terminal disclaimer filed on September 13, 2006 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent 5,387,676 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Rejections necessitated by Rejoinder

The following rejections are new rejections applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant process claims contain allowable product inventions. Per Applicant's written request for rejoinder filed on September 13, 2006 and in accordance with MPEP §821.04, the process claims are currently under examination.

The claims are drawn to a method of blocking *in vivo* expression of the MN gene in a human by administering an MN antisense construct (claim 39) and a method of treating neoplastic disease in a human by administering an MN antisense construct (claim 40). Accordingly, the instant claims read only on the *in vivo* application of MN antisense constructs in humans.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not

be undue experimentation. The key word is 'undue', not 'experimentation'." (Wands, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

As neither antisense therapeutics nor clinical trials are performed routinely in the art, to determine whether the MN antisense construct comprising a complementary sequence of SEQ ID NO:5 would effectively inhibit the expression of the MN gene in a human subject would require undue experimentation. The claimed invention must be enabled at the time of the effective filing date, which antedates to the year of 1992 when the antisense therapeutics as well as DNA-based therapeutics as a whole were nascent and the clinical data proving the efficacy of such therapeutics were meager. The unpredictable therapeutic effects of DNA-based drugs for human use are still unresolved and addressed by Patil et al's comprehensive review (*The AAPS Journal,* 2005, 7:E61-E77).

On page E62, Patil et al. teach the complications of using DNA-based drugs as following:

"The innate ability of DNA-based drugs to be internalized by target cells is minimal under normal circumstances. In addition, poor biological stability and a short half-life result in unpredictable pharmacokinetics. Furthermore, DNA molecules that do manage to enter the cell are subsequently subjected to intracellular degradation along with stringently restricted nuclear access. The resulting random delivery profile of DNA-based drugs is further complicated by a lack of in vivo/in vitro correlation of their pharmacological outcomes."

Moreover, the instant specification does not provide any working examples or guidance/direction as to how to practice the instantly claimed invention *in vivo* in humans.

As such, one of ordinary skill in the art would not be able to predict the therapeutic outcomes of the MN antisense construct in the absence of clinical data. The unpredictable pharmacokinetics of DNA-based drugs as taught by Patil et al. thus would necessitate undue experimentation for one skilled in the art to ascertain the therapeutic effects of treating neopalstic diseases *in vivo* in human subjects.

In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991), the Court ruled that a rejection under 35 U.S.C. 112, first paragraph for lack of enablement was appropriate given the relatively incomplete understanding in the biotechnological field involved, and the lack of a reasonable correlation between the narrow disclosure in the specification and the broad scope of protection sought in the claims.

In view of the foregoing, one skilled in the art cannot predict that the claimed method of blocking the MN gene expression and treating neoplastic diseases in humans will be effective, if the MN antisense construct was administered to humans, particularly since the specification has not set forth any working examples in humans. It is well known that the art of nucleic acid-based drug discovery for therapy is highly unpredictable as stated above. Accordingly, it is clear that based on the state of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the method drawn to blocking the MN gene expression and treating neoplastic diseases in humans comprising administering the MN antisense construct of claim 31 would be used without undue experimentation.

Conclusion

Claims 31-35 and 53-55 are in condition for allowance, contingent upon the approval of the terminal disclaimer over U.S. Patent 5,387,676.

Claims 39-40 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

TC 1600
JANE ZARA, PH.D.
PRIMARY EXAMINER